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Y1-09 **Young Investigators Day, Sat, Sept 1, 08:30 - 16:40**

The case for surgery in very early disease

Tsuboi, Tsuboi Kato, Harubumi

Tokyo Medical University & Hospital, Tokyo, Japan

In 2001, the Japanese Joint Committee of Lung Cancer Registry sent a questionnaire to 320 Japanese institutions regarding the prognosis and clinicopathological profiles of patients who underwent the resection for primary lung neoplasms in 1994. We compiled the data for 7408 patients from 303 institutions (94.7%). Among these, 6644 patients with non-small cell histology were studied in terms of prognosis. The 5-year survival rate of the entire group was 52.6%. The 5-year survival rates by clinical (c-) stage were as follows: 72.1% for IA (n = 2423), 49.9% for IB (n = 1542), 48.7% for IIA (n = 150), 40.6% for IIB (n = 746), 35.8% for IIIA (n = 1270), 28.0% for IIIB (n = 366) and 20.8% for IV (n = 147). The difference in prognosis between neighboring stages was significant except for between IB and IIA and between IIIB and IV. The 5-year survival rates by pathological (p-) stage were as follows: 79.5% for IA (n = 2009), 60.1% for IB (n = 1418), 59.9% for IIA (n = 232), 42.2% for IIB (n = 757), 29.8% for IIIA (n = 1250), 19.3% for IIIB (n = 719) and 20.0% for IV (n = 259). The difference in prognosis between neighboring stages was significant except for between IB and IIA and between IIIB and IV. The survival curves of stages IB and IIA were almost superimposed in both c- and p-settings. Otherwise, the present TNM staging system seemed to well characterize the stage-specific prognosis in non-small cell lung cancer. The T1 descriptor definition and stage grouping for testing was revised as follows. According to the greatest tumor diameter, T1 tumors were divided into T1a tumors (< or =2.0 cm) and T1b tumors (2.1-3.0 cm). With these descriptors, new IA and IB stages were defined as T1a N0 M0, T1b N0 M0, and T2 N0 M0, respectively. For 6644 patients with histologically non-small cell lung cancers resected in 1994 and reported in the Japanese Lung Cancer Registry Study, the survivals and prognostic difference between neighboring stages were studied. The 5-year survival of the entire population was 52.6%. In the clinical setting, the 5-year survivals of the new IA, new IB stages were 77.5% and 69.3%, respectively. In the pathologic setting, they were 83.7% and 76.0%, respectively. For both clinical and pathologic settings, differences between all neighboring stages were statistically significant. Subcategorization of T1 and minor changes in stage grouping results in a system with significant differences in prognosis between neighboring stages. Additionally, the definition of "non-invasive peripheral early cancer" will be reported by Japanese collaboration study in this session

Y1-10 **Young Investigators Day, Sat, Sept 1, 08:30 - 16:40**

Adjuvant therapies: what we have learned in the last 5 years

Scagliotti, Giorgio V. Selvaggi, Giovanni

University of Torino, Orbassano, Italy

Following the results of a meta-analysis published 15 years ago, which showed a 5-year survival benefit of approximately 5% for adjuvant chemotherapy in patients with non-small cell lung cancer (NSCLC) [1], various large multicentre studies have investigated the benefit of adjuvant chemotherapy in this disease.

The findings of the above mentioned meta-analysis failed to impact clinical practice, not because the absolute gain was too small but because such an estimate was still imprecise, ranging from 1% detriment to a 10% benefit. In addition, the heterogeneity of surgical procedures and the difference in the staging modalities strongly limit the applicability of the results of this meta-analysis.

Recently published results of five such studies suggest that adjuvant chemotherapy improves survival in patients with stage IIIA and II disease, but not in stage I disease [2-6].

These conclusions have been further supported by a recent meta-analysis of individual patient data - the Lung Adjuvant Cisplatin Evaluation (LACE) - from five large studies (ALPI, ANITA, IALT, JBR.10 and Big Lung Trial [BLT]) [7]. This analysis involved data from 4,584 patients with resected NSCLC who were randomized to adjuvant chemotherapy chemotherapy or no further systemic therapy. In some of these studies, adjuvant radiotherapy was used and left to the discretion of each participating centre. Adjuvant chemotherapy was associated with a significant benefit in overall survival; at 5 years, there was a 5.3% ± 1.6% absolute increase in survival in favor of adjuvant chemotherapy compared with no further systemic therapy. The overall benefit observed varied with stage; there was a significant benefit for patients with stage II and stage III disease whereas there was no significant benefit for those with stage IB disease and an apparent detrimental effect for those with stage IA disease.

In contrast to the findings above, a meta-analysis of several Japanese studies of post-operative adjuvant chemotherapy reported a survival benefit in patients with stage I disease [8]. Of the 2,003 patients studied, 95% had stage I disease. Patients were randomized to receive an oral adjuvant treatment with tegafur in combination with uracil (UFT) for 2 years or no further treatment. The overall survival rates at 5- and 7-years were significantly greater in patients who had received adjuvant chemotherapy than in those who had received surgery alone (81.8% vs 76.5% at 5 years, p = 0.011; 77.2% vs 69.5% at 7 years, p = 0.001).

The concept of relatively mild, low-dose continuous adjuvant therapy is attractive, but the absence of confirmatory adjuvant UFT studies outside Japan strongly limit the applicability of these data in clinical practice because of potential pharmacogenomic differences between Japanese and non-Japanese patients.

In two of the positive studies for adjuvant chemotherapy [4,6], a combination of cisplatin and weekly vinorelbine prolonged survival. These findings led to the conclusion that cisplatin/vinorelbine is a regimen of choice for adjuvant therapies. However, in another adjuvant trial, the combination of cisplatin and vinorelbine did not perform significantly better than any other combination tested [2]. Moreover, when the combination of cisplatin plus a third-generation agent including taxanes, vinorelbine and gemcitabine are compared 'head to head' in the metastatic or locally advanced settings, no significant differences in overall survival are observed.